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FILE 'CAPLUS' ENTERED AT 10:52:25 ON 30 OCT 2003

FILE COVERS 1907 - 30 Oct 2003 VOL 139 ISS 18
FILE LAST UPDATED: 29 Oct 2003 (20031029/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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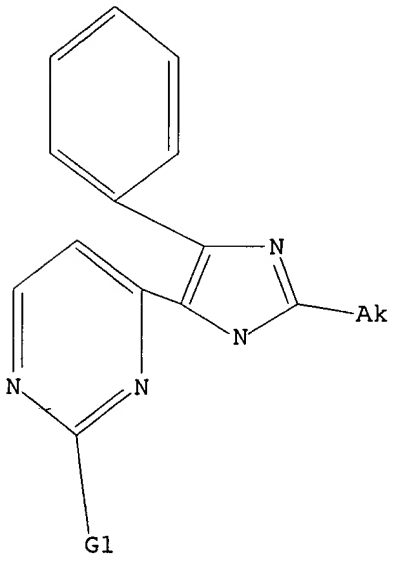

G1 N,X

Structure attributes must be viewed using STN Express query preparation.
L3 20 SEA FILE=REGISTRY SSS FUL L1
L4 2 SEA FILE=CAPLUS L3

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L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:396863 CAPLUS
DOCUMENT NUMBER: 135:19656
TITLE: Preparation of 4-[pyridin-4-yl(or pyrimidin-4-yl)]-1H-

imidazoles as B-Raf kinase inhibitors

INVENTOR(S): Dean, David Kenneth; Lovell, Peter John; Takle, Andrew Kenneth

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK

SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038324	A2	20010531	WO 2000-GB4413	20001120
WO 2001038324	A3	20020510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1232153	A2	20020821	EP 2000-977660	20001120
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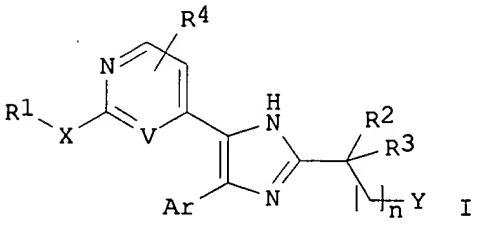
JP 2003514906	T2	20030422	JP 2001-540087	20001120

PRIORITY APPLN. INFO.:

US 1999-166814P	P	19991122
US 1999-166885P	P	19991122
US 1999-166886P	P	19991122
US 1999-166895P	P	19991122
WO 2000-GB4413	W	20001120

OTHER SOURCE(S): MARPAT 135:19656

GI



I

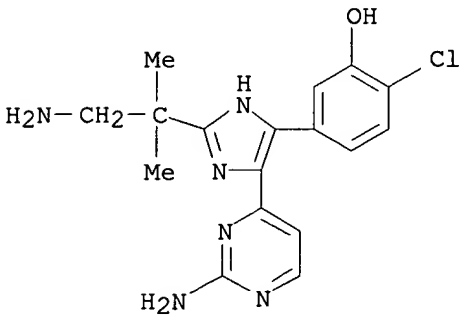
AB The title compds. [I; X = O, CH2, S, NH, or XR1 = H; V = CH, N; Y = NR10R11, NR10C(:Z)NR10R11, NR10CO2R11, NR10SO2R11; Ar = (un)substituted Ph, 5-6 membered heteroaryl; n = 0-4; R1 = H, alkyl, aryl, etc.; R2, R3 = alkyl, or R2 and R3 together with the carbon atom to which they are attached form (un)substituted cycloalkyl, cycloalkenyl, 5-7 membered heterocyclyl; R4 = H, halo, etc.; R10, R11 = H, alkyl, etc.; Z = O, S], useful as B-Raf kinase inhibitors for the treatment of neurotraumatic diseases, were prepd. E.g., a multi-step synthesis of I [XR1 = H; V = CH; Y = NHCO2tBu; n = 1; Ar = 4-Cl-3-MeOC6H3; R2, R3 = Me; R4 = H] was given. The exemplified compds. I were found to be effective in inhibiting B-Raf mediated phosphorylation of GST-kdMEK substrate having IC50's of < 3 .mu.M.

IT **342434-87-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-[pyridin-4-yl(or pyrimidin-4-yl)]-1H-imidazoles as B-Raf kinase inhibitors)

RN 342434-87-1 CAPLUS

CN Phenol, 5-[2-(2-amino-1,1-dimethylethyl)-5-(2-amino-4-pyrimidinyl)-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



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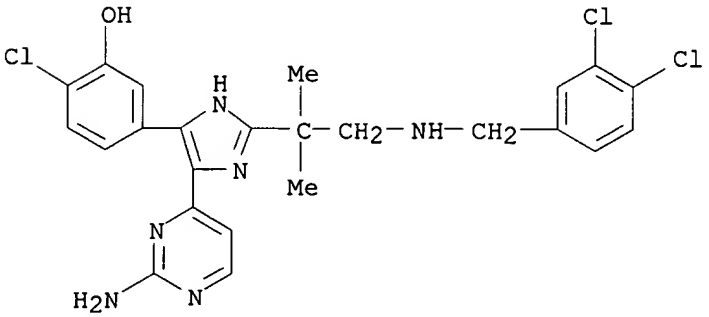
342434-91-7P 342434-92-8P 342434-93-9P
342434-94-0P 342434-95-1P 342434-96-2P
342434-97-3P 342434-98-4P 342434-99-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-[pyridin-4-yl(or pyrimidin-4-yl)]-1H-imidazoles as B-Raf kinase inhibitors)

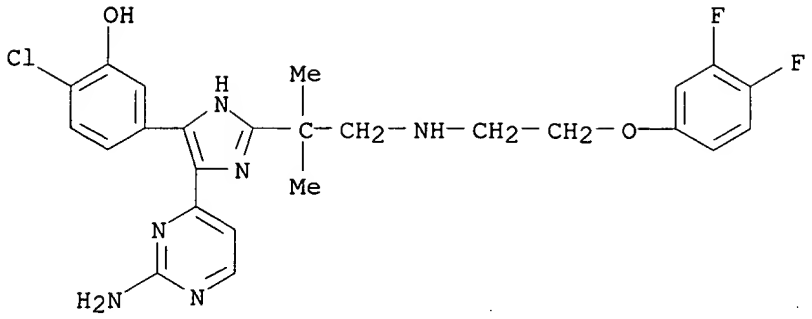
RN 342434-88-2 CAPLUS

CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[(3,4-dichlorophenyl)methyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)

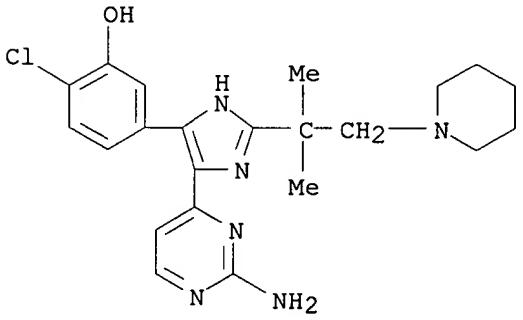


RN 342434-89-3 CAPLUS

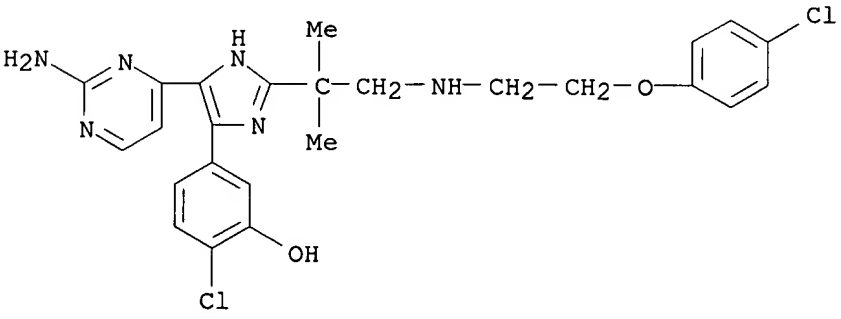
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[2-(3,4-difluorophenoxy)ethyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



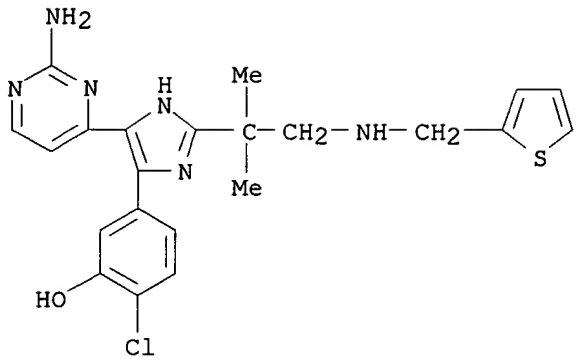
RN 342434-90-6 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[1,1-dimethyl-2-(1-piperidinyl)ethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



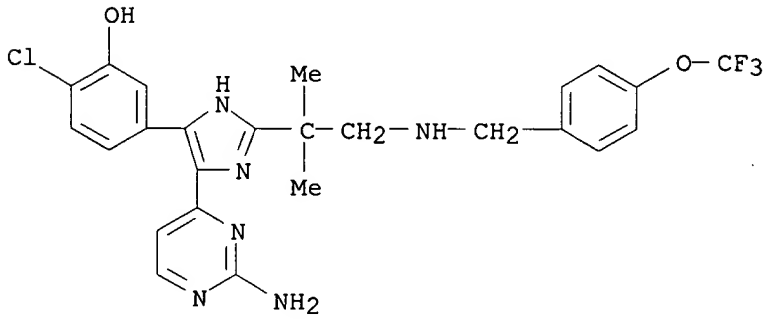
RN 342434-91-7 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[2-(4-chlorophenoxy)ethyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



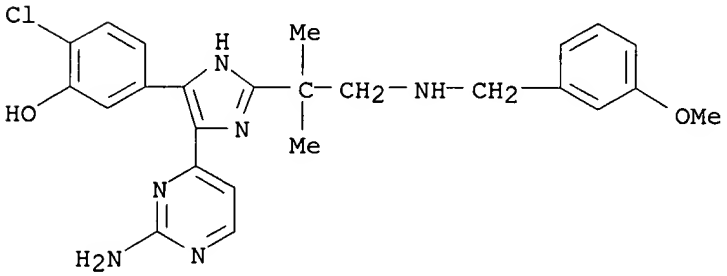
RN 342434-92-8 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[1,1-dimethyl-2-[(2-thienylmethyl)amino]ethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



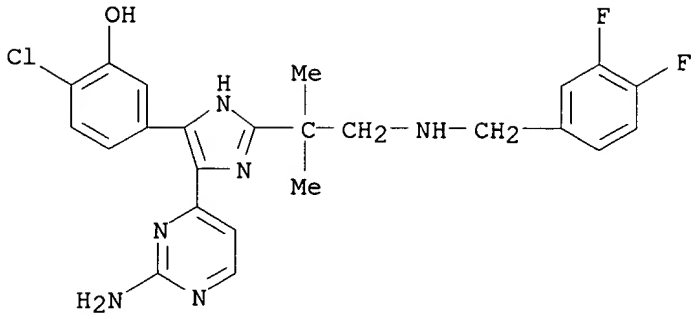
RN 342434-93-9 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[1,1-dimethyl-2-[[[4-(trifluoromethoxy)phenyl]methyl]amino]ethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



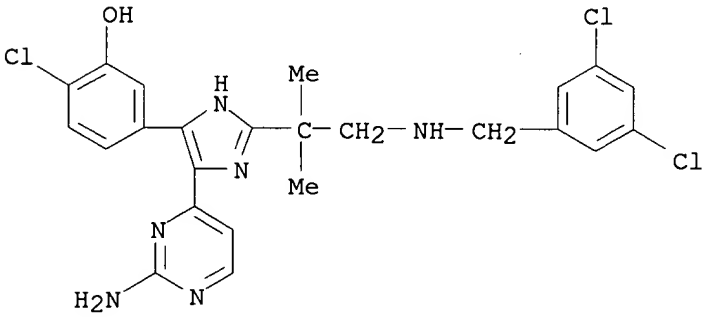
RN 342434-94-0 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[(3-methoxyphenyl)methyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



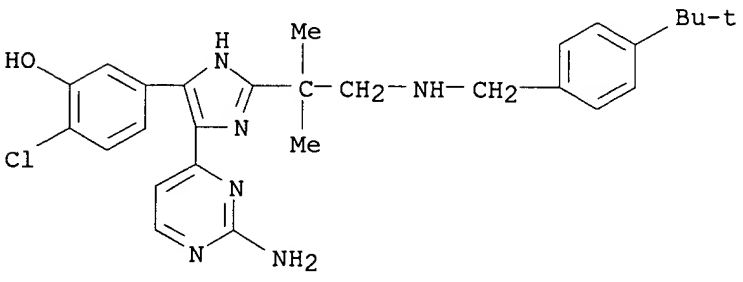
RN 342434-95-1 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[(3,4-difluorophenyl)methyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



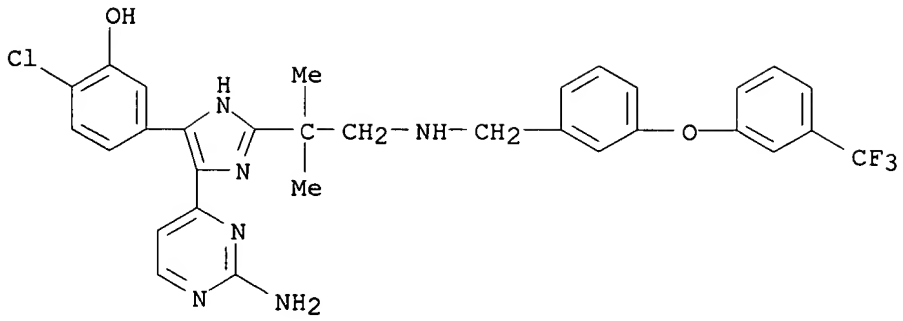
RN 342434-96-2 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[(3,5-dichlorophenyl)methyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



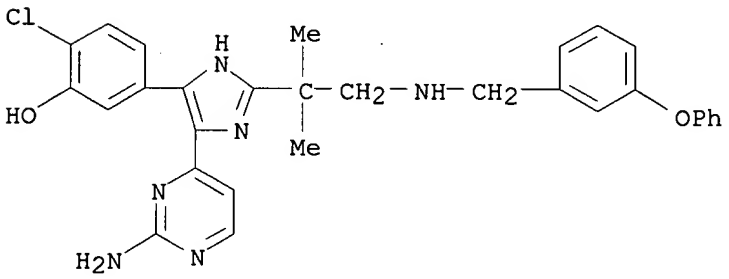
RN 342434-97-3 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[2-[[[4-(1,1-dimethylethyl)phenyl]methyl]amino]-1,1-dimethylethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



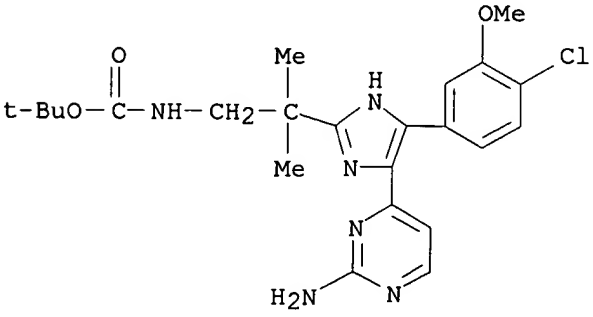
RN 342434-98-4 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[1,1-dimethyl-2-[[[3-[3-(trifluoromethyl)phenoxy]phenyl]methyl]amino]ethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



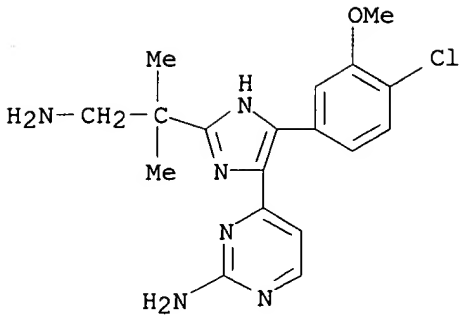
RN 342434-99-5 CAPLUS
CN Phenol, 5-[5-(2-amino-4-pyrimidinyl)-2-[1,1-dimethyl-2-[[(3-phenoxyphenyl)methyl]amino]ethyl]-1H-imidazol-4-yl]-2-chloro- (9CI) (CA INDEX NAME)



IT **342435-21-6P 342435-22-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-[pyridin-4-yl(or pyrimidin-4-yl)]-1H-imidazoles as B-Raf kinase inhibitors)
RN 342435-21-6 CAPLUS
CN Carbamic acid, [2-[4-(2-amino-4-pyrimidinyl)-5-(4-chloro-3-methoxyphenyl)-1H-imidazol-2-yl]-2-methylpropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 342435-22-7 CAPLUS
CN 2-Pyrimidinamine, 4-[2-(2-amino-1,1-dimethylethyl)-5-(4-chloro-3-methoxyphenyl)-1H-imidazol-4-yl]- (9CI) (CA INDEX NAME)

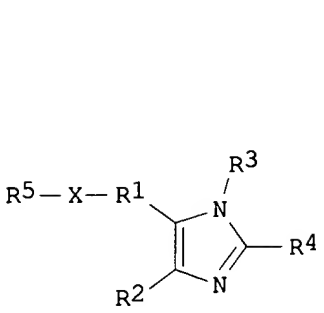


L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:314693 CAPLUS
DOCUMENT NUMBER: 132:321861
TITLE: Anti-inflammatory 4-phenyl-5-pyrimidinyl-imidazoles and their preparation, compositions, and use
INVENTOR(S): Revesz, Laszlo
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026209	A1	20000511	WO 1999-EP8358	19991102
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964765	A1	20000522	AU 1999-64765	19991102

PRIORITY APPLN. INFO.:
GB 1998-24063 A 19981103
GB 1999-3440 A 19990215
WO 1999-EP8358 W 19991102

OTHER SOURCE(S): MARPAT 132:321861
GI



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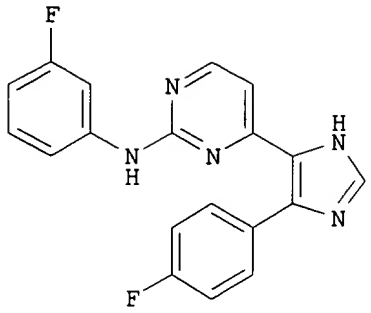


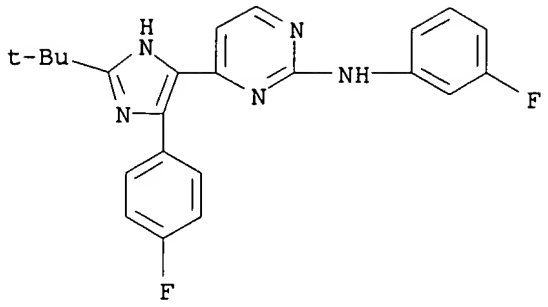
II

AB Novel 4-phenyl-5-[2-(Y-X)-4-pyrimidinyl]imidazoles [Y = aryl, cycloalkyl, aralkyl, or cycloalkylalkyl; X = N, O, S] and their pharmaceutically acceptable and cleavable esters and acid addn. salts are provided. In particular, compds. I and their esters and salts are disclosed [wherein R1 = pyrimidinyl; X = NR6Y, O, S; R6 = H, alkyl, aryl, heteroaryl, aralkyl, or heteroaralkyl; Y = alkylene or bond; R2 = (un)substituted Ph; R3 = H, heterocyclyl, heterocyclylalkyl, (un)substituted alk(en/yn)yl, cycloalkyl, aryl, etc.; R4 = H, (un)substituted alkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; R5 = (un)substituted aryl, heteroaryl, or cycloalkyl]. The compds. are MAP kinase inhibitors, useful pharmaceutically for treating TNF.alpha. and IL-1 mediated diseases such as rheumatoid arthritis and diseases of bone metab., e.g., osteoporosis. Use of the compds. as antiinflammatory and immunosuppressant agents is specifically claimed. For example, 4-methyl-2-(methylthio)pyrimidine was lithiated with BuLi and C-acylated with 4-fluoro-N-methoxy-N-methylbenzamide to give 65% 4-fluoro-2'-(2-methylthio-4-pyrimidinyl)acetophenone. The latter underwent .alpha.-bromination (100%), cyclization with formamide and ammonium formate to give an imidazole (38%), S-oxidn. with mCPBA to give the sulfoxide (70%), and substitution reaction with 3-fluoroaniline (18%) to give title compd. II. The compds. had typical IC50 values of 100 nM to 10 nM or less in a p38 MAP kinase inhibition assay, and gave up to approx. 50% inhibition of TNF prodn. in LPS-stimulated mice at 10 mg/kg orally.

IT **266357-93-1P**, 4-(4-Fluorophenyl)-5-[2-(3-fluorophenylamino)-4-pyrimidinyl]-2-tert-butylimidazole **266358-00-3P**, (R)-5-(4-Fluorophenyl)-2-(1-amino-1-methylethyl)-4-[2-[1-phenylethylamino]-4-pyrimidinyl]-1H-imidazole **266358-01-4P**, (S)-5-(4-Fluorophenyl)-2-(1-amino-1-methylethyl)-4-[2-[1-phenylethylamino]-4-pyrimidinyl]-1H-imidazole **266358-02-5P**, 5-(4-Fluorophenyl)-2-(1-amino-1-methylethyl)-4-(2-cyclohexylamino-4-pyrimidinyl)-1H-imidazole **266358-03-6P**, 5-(4-Fluorophenyl)-2-(1-amino-1-methylethyl)-4-[2-[(cyclopropylmethyl)amino]-4-pyrimidinyl]-1H-imidazole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of phenylpyrimidinylimidazoles as antiinflammatories and immunosuppressants)

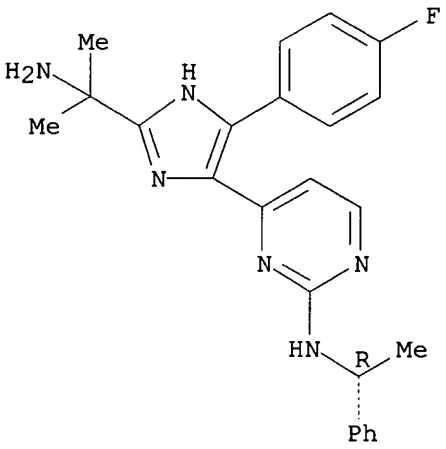
RN 266357-93-1 CAPLUS

CN 2-Pyrimidinamine, 4-[2-(1,1-dimethylethyl)-5-(4-fluorophenyl)-1H-imidazol-4-yl]-N-(3-fluorophenyl)- (9CI) (CA INDEX NAME)



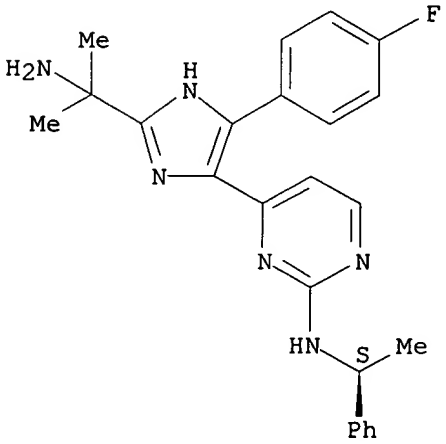
RN 266358-00-3 CAPLUS
CN 2-Pyrimidinamine, 4-[2-(1-amino-1-methylethyl)-5-(4-fluorophenyl)-1H-imidazol-4-yl]-N-[(1R)-1-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 266358-01-4 CAPLUS
CN 2-Pyrimidinamine, 4-[2-(1-amino-1-methylethyl)-5-(4-fluorophenyl)-1H-imidazol-4-yl]-N-[(1S)-1-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 266358-02-5 CAPLUS
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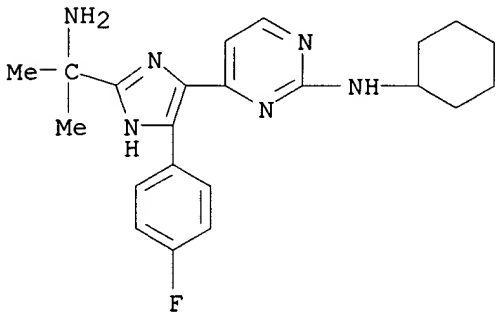

RN 266358-03-6 CAPLUS
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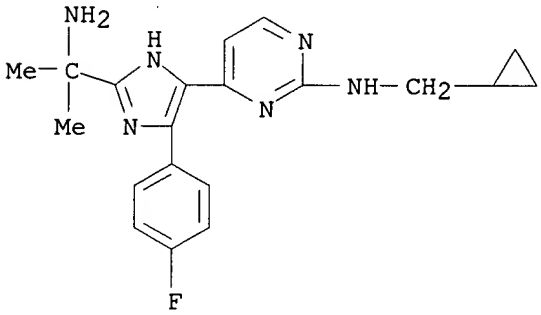

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT